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wherein m is 1 or 2;

R<sub>4</sub> is a hydroxyl group, or a protected hydroxyl group; and

R<sub>5</sub> is H or an amino protecting group;

provided that when said compound has formula XVIIID, q is at least 1.

#### REMARKS

After entry of the proposed amendment, claims 1-6, 8-20, 32, 33, 35, 40, 42-44, 63-68, 72, 79-81 and 88-109 will be pending.

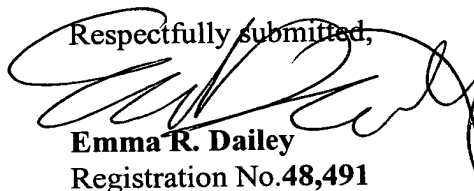
The claims have been amended to require q for such formulas denoted "D" in the claims to be at least one. In addition, the definition of R<sub>4</sub>, which may be found, for example, in the specification on page 12 at line 14, has been added where appropriate. The obvious typographical error in claim 45 through which XIIB was inadvertently substituted for XIIIB has also been corrected. In addition, the obvious typographical error through which R<sub>40</sub> was inadvertently substituted for R<sub>41</sub> has been rectified throughout the specification and claims.

Those of ordinary skill in the art would appreciate that the amendment to claims 31, 38 and 41 (new claims 104-106) merely provides clarification for the otherwise inherent characteristic of the linking group represented by W<sub>1</sub>; *i.e.*, that of possessing a moiety, such as hydrogen, that is available to react when forming the linkage.

**DOCKET NO.: ISIS-4803**

**PATENT**

In view of the foregoing, Applicants respectfully submit that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,  
  
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**VERSION WITH MARKINGS TO SHOW CHANGES****In the Specification**

On page 1, under the heading "Cross-Reference," please delete the first full paragraph (starting on line 3 and ending on line 5) and insert the paragraph provided below:

[This application is a continuation-in-part application of U.S. Application Serial No. 09/098,166, filed June 16, 1998.]

This patent application is a divisional of U.S. Application Serial No. 09/275,505, filed March 24, 1999, which is a continuation-in-part of U.S. application serial no. 09/098,166, filed June 16, 1998, which is a continuation in part of U.S. application serial no. 08/117,363, filed September 3, 1993.

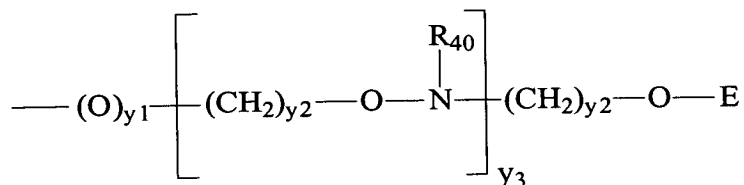
On page 48 before the "DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS" section, please add the following text in the "BRIEF DESCRIPTION OF THE DRAWINGS" section:

Figure 21 shows the structures of compounds 79a and 79b.

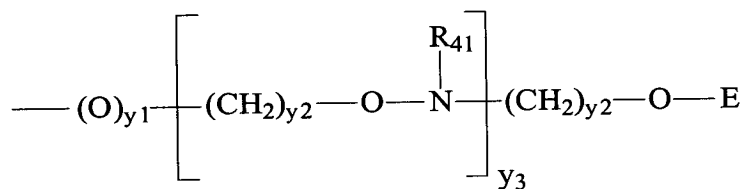
Figure 22 shows the structures of compounds 80a, 80b, 81b, 82a and 82b.

Figure 23 shows the structures of compounds 83a, 83b, 84b, 85a and 86a.

In the Specification each of ten separate places, on page 17 at line 1, and on page 26 at line 1, and on page 30 at line 1, and on page 32 at line 1, and on page 40 at line 14, and on page 54 at line 1, and on page 62 at line 1, and on page 66 at line 1, and on page 68 at line 9, and on page 78 at line 14, and in claims 7, 21-23, 45, 73 and 82, please replace the formula



with the following formula:



### In the Claims

Please cancel claims 7, 21-31, 34, 36-39, 41, 45-62, 69-71, 73-78 and 82-87, without prejudice. Please amend claims 8-12, 32, 35, 40, 42, 63, 65, 79, 88, and add claims 101-109 as presented below in amended form:

In claims 8-12 and 93, please replace "7" with "101"

In claim 32, please replace "31" with "104".

In claim 42, please replace "26" with "41".

In claim 63, please replace "62" with "107".

In claim 79, please replace "78" with "108".

In claim 88, please replace "82" with "109".

35. (Amended) The method of claim [31] 104 wherein  $R_1$  is dimethoxytrityl, A has the formula  $-O-(CH_2)_n-NH-$  where n is 6, m is 2,  $R_4$  is t-butoxy,  $R_5$  is trifluoroacetyl,  $R_6$  is  $-C(=O)-CH(CH_3)_2$ , and  $R_{30}$  is [FMOC] FMOX.

40. (Amended) The method of claim [38] 105 wherein  $R_1$  is dimethoxytrityl,  $W_1$  has the formula  $-O-(CH_2)_n-NH-$  where n is 6, m is 2,  $R_4$  is t-butoxy,  $R_5$  is trifluoroacetyl,  $R_6$  is  $-C(=O)-CH(CH_3)_2$ , and  $R_{30}$  is [FMOC] FMOX.

65. (Amended) The compound of claim [54] 64 wherein  $R_4$  is t-butoxy.